REMARKS

Claims 1-4 are all the claims pending in the application. After entry of the present Amendment, claims 1 and 2 will be canceled, claim 3 will be amended, and claim 5 will be a new claim in the application.

Claim 3 has been amended to further recite the selective nature of the compound described in the claim (supported at page 6, line 22 – page 7, line 6), and the inclusion of a carrier in the pharmaceutical composition.

Claim 5 is fully supported by the specification, see for example, page 22, lines 4-16.

Accordingly, no new matter has been added and entry of this amendment is respectfully requested.

I. Formal Matter

The Examiner returned an initialed and signed copy of the Form PTO 1449, submitted by Applicants on August 2, 2000, with the Office Action dated January 29, 2000. However, the Examiner did not indicate that he reviewed JP 8-169884 (i.e. it was not initialed). Therefore, Applicants include with the present filing a copy of the Form PTO 1449 and request that the Examiner indicate JP 8-169884 was made of record by initialing this citation, and returning a copy of the signed form to Applicants.

II. Rejection of Claims under 35 U.S.C. §102(b)

On page 2 of the Office Action, the Examiner rejects claims 1-4 under 35 U.S.C. §102(b) as being anticipated by the Japanese Patent Application 8-169884.

The Examiner asserts that the Japanese patent application teaches the use of the claimed compounds in a pharmaceutical formulation.

In response, the Applicants note that the present invention relates to a composition for treating cerebral infarction which comprises a compound having mGluR1 antagonism as an active ingredient. The use of the compound to treat a cerebral infarction according to the present invention is based on the ability of the claimed compound to inhibit acute neuronal cell death. JP-A-8-169884 cited by the Examiner may disclose a compound having mGluR1 antagonism and describe that the compound is useful for improving/treating the aftereffects of the cerebral infarction. However, Applicants assert that the reference does not teach or suggest an agent for treating the cerebral infarction by using a selective mGluR1 antagonist.

In addition, although the reference discloses that glutamate receptors participate in the delayed neuronal cell death (line 3 of paragraph [0002]), there is no clear description as to how mGluR1 antagonists influence neuronal cell death.

Cozzi et al. reported that a mGluR1 antagonist reduced the loss of pyramidal cells which are found in the CA1 area of the hippocampus from four days after ischemia in a global cerebral ischemia model (Society for Neuroscience Abstracts 23, 788.2 (1997)).

Ferraguti et al. reported that, in a local permanent occlusion model (MCAO) using an inactivated mGluR1 mutant mouse, the ischemic infarct observed seven days after the infarction was not different between the mGluR1 mutant mouse and the wild-type mouse (but tended to increase) (Neuroscience 7(1) 1-5 (1997)).

In contrast, Henrich-Noack et al. state in Neuroreport 9:985-988 (1998) that they reported in 1997 that 4CPG, which is a selective Group I mGluR1 antagonist, did not inhibit hippocampal neuronal cell death after transient ischemia (Abstract book of the XXXIII International Congress of Physiological Sciences, June 30-July 5 in St. Petersburg (1997)). In other words, they reported a result which is opposite to the report by Cozzi et al.

From the above reports, it is clear that at the time when the present invention was made, there had been no teaching or suggestion about the ability of selective mGluR1 antagonists to treat cerebral infarction based on their ability to inhibit acute neuronal cell death.

Accordingly, the present invention has an effect which is not taught or suggested by JP-A-169884. Thus, the present invention is unobvious.

III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

The paragraph encompassed by page 2, line 25 through page 3, line 4:

Though metabotropic glutamate receptors appear ~~are appeared~~ to be a significant component in the cascades following excessive glutamate release during and after cerebral ischemia, their roles are not yet clear. Particularly, as the activation of mGluR1 and mGluR5 which is coupled to intracellular IP3 system increases intracellular calcium (Nature, 383, 89-92 1996), continuous excess stimulation of these receptors may cause neuronal cell death.

The paragraph encompassed by page 3, lines 5-18:

Regarding the neuroprotective effect of compounds having mGluR1 antagonism in cerebral ischemia, Cozzi ~~Cozz~~ et al. reported that intraventricular administration of AIDA ((RS)-1-aminoindan-1,5-dicarboxylic acid) reduced the loss of the neuronal cells found in the CA1 area of ~~in~~ gerbils ~~which~~ exposed to 5 min of cerebral ischemia (Society for Neuroscience Abstracts, vol. 23, 788.2, 1997). However, Henrich-Noack et al. reported that 4C3HPG ((S)-4-carboxy-3-hydroxyphenylglycine), which is an antagonist of ~~at~~ the Group I mGluRs and an agonist of ~~at~~ Group II mGluRs, is effective, but 4CPG ((S)-4-carboxyphenylglycine), which is a selective Group I mGluR ~~mGluRs~~ antagonist is not effective in the same model (Society for Neuroscience Abstracts, vol. 23, 756.8, 1997).

The paragraph encompassed by page 3, lines 19-25:

One of the reasons for this ~~these~~ discrepancy is considered to be due to the insufficient efficacy and selectively of mGluR1 antagonists used in these experiments. Therefore, it is considered that the neuroprotective effect of compounds having mGluR1 antagonism in cerebral ischemia is not clearly confirmed.

The paragraph encompassed by page 19, lines 22-24:

Next, the invention is described further in detail based on examples, though the invention is not limited to these examples.

IN THE CLAIMS:

Claims 1 and 2 are canceled.

The claims are amended as follows:

3. A ~~The~~ pharmaceutical composition for treating cerebral infarction~~according to claim 1~~, which comprises a compound having selective mGluR1 antagonism as an active ingredient in a pharmaceutically effective amount.

Claims 5-8 are added as new claims.